Testimony

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Setting the Path for Reauthorization: Improving Portfolio Management at NIH

Statement of

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Throughout history, the toll of suffering from disease and injury on individuals and societies has been a constant and unforgiving reminder of the human condition. We have never stopped trying to overcome this suffering. Our goal is to help people, regardless of age, gender, race, or nationality. The torment of those who are afflicted by illness is the main reason that medical research is one of America's top priorities.

Since the mid-twentieth century, the National Institutes of Health (NIH), currently the largest supporter of biomedical research in the world, has been the pilot and engine of the machine that drives biomedical research. Congress's investment in NIH has paid quantifiable human health dividends. We have come far in our quest for discoveries that lead to improvements in diagnostics, prevention therapies, disease or condition management, and actual cures. Life expectancy continues to rise steadily; death from heart disease and stroke has sharply declined; cancer mortality has fallen while survivability increases; vaccines and drug therapies have proliferated - we can expect these and other improvements in human health to accelerate as a result of advances in genomics, molecular biology, proteomics, and computational biology.

Yet as far as we have come in our journey, we still have a seemingly infinite and difficult road to traverse. We understand perhaps ten percent or less of the human biology necessary for the prevention, diagnosis, and treatment of disease and injury. Our understanding of the molecular underpinnings of cells and other aspects of human biology offer promising theoretical applications for medical treatment, but years of research efforts lie ahead before theories are translated to concrete discoveries. The challenge of emerging and reemerging infectious diseases will not lessen. The difficulty of treating chronic illnesses is a persistent dilemma.

Health disparities continue to affect segments of our population. The threat of bioterrorism represents yet another challenge.

These challenges are a reminder that NIH must continue to strive to improve, to seek innovations, and to constantly subject itself to review and examination. As I testified before this Subcommittee on June 2, 2004, "Great organizations can maintain greatness only by continuous reassessment and adaptation." Or as the Institute of Medicine observed two years ago, "While NIH's success is to be celebrated, success alone does not answer fully the question of whether there is a better way to proceed, particularly as one faces a future where the world of biomedical science is being rapidly transformed in virtually all its dimensions."

To meet these challenges, the NIH works very hard to maintain a research portfolio that balances public health needs and scientific opportunities. We seek input through multiple channels, both formal and informal, and maintain an open door policy for communication with our stakeholders. Ideas for scientific initiatives in specific areas of science come from many sources – advocacy groups, the biomedical research community, Congress, and NIH staff, among others. Ideas for stimulating a particular field or letting it lie fallow become reality only after rigorous vetting at a number of levels.

The NIH's two-tiered peer review system, which is world-renowned and respected, has a major influence in the priorities set by NIH. In this system, the assessment of the scientific and technical merit of an application is separate from its consideration for funding. In the first level, the peers of the applicant assess the application's scientific and technical merit. Advisory

councils and boards, which consist of senior scientific experts and lay members of the public, provide the second level of review - advice and recommendations to the Institutes and Centers on the programmatic relevance of the applications and areas of science that should be emphasized (or not). Advisory councils and boards are also, however, the NIH's top vetting place for ideas for scientific initiatives that will receive set-aside funds, and they are expected to provide advice on the Institute's or Center's scientific priorities.

NIH's priorities are driven, in part, by the ideas and opportunities presented to us through the grant applications we receive. By placing most of our resources in investigator-initiated peer-reviewed research, NIH ensures that federal dollars support the latest and best science. But the ideas generated by the scientific community represent only one factor in a complex, multifaceted process. Some of the variables in choosing resource allocations include public health needs such as the burden of disease, new scientific opportunities, the quality of research proposals, the experience of applicants, and the ability to sustain research through adequate staffing and infrastructure. These factors are often lost in the public debate about NIH funding, in which the discussion is sometimes simplified by focusing attention on apparent differences between the toll of certain diseases and the amount spent on research about those diseases.

While I believe this process has served the public well – in fact, there is evidence that NIH priorities match well with existing disease burdens – we can do better. Currently, many priorities are set by the planning programs at each of the Institutes and Centers at NIH that support research grants. In recent years, NIH has facilitated collaborations and co-funded innovative trans-Agency research. In the case of HIV/AIDS research, we are shifting resources

to fund vaccine research to respond to urgency as well as opportunity. As scientific fields and disciplines are increasingly becoming interdependent and advances in one area often make progress possible in another, NIH needs a horizon view of our research portfolio – a view that complements and oversees the views of the individual Institutes and Centers with very specific mission areas.

It is not only the nature of science that is changing. The condition of our patients has evolved differently as well. Our success in prolonging life and treating acute diseases means that more patients are living with chronic and multiple illnesses. Our treatment methods must adapt to older patients with multiple symptoms just as our methods of conducting research must adapt to changes in science.

I testified before this Subcommittee last year that we cannot be static, that NIH must enhance the current process for determining priorities and allocating resources as part of a balanced research portfolio across the Agency and within each Institute and Center. I noted that the system of funding research by allocating resources directly to disease, organ, or special population-based Institutes and Centers has been successful. I also observed that science is changing, driven by new technologies and discoveries. Modern research is often best conducted by teams, which may include biologists, mathematicians, chemists, physicists, engineers, bioimagers, computer scientists, behavioral scientists, and physicians, and which may cut across the expertise of many different NIH Institutes and Centers. Several fertile areas of research - genomics, proteomics, molecular engineering - serve all fields of endeavor and cannot be pigeonholed or accounted for according to specific diseases.

I told you that I was thinking about ways to refine the priority setting process and the management of our portfolio. In particular, I have been examining new and sustained approaches for evaluating NIH's crosscutting science. While maintaining the support for existing Institute and Center research programs, we are now using trans-NIH resources to address emerging challenges and opportunities. These new areas of investment involve research that no single Institute can support alone, but that all of NIH needs to pursue because of the impact on all diseases and scientific areas of inquiry.

I understand the questions about priority setting at NIH that many have. There are several factors to be considered as we ponder the answers.

- Our challenges are different. The burden of illness has shifted from acute to chronic diseases as health care costs rise and the population ages.
- As the Institute of Medicine concluded, *"The frontier of biomedical science has rarely been as exciting and as full of spectacular opportunities as it is today. From basic science through clinical research to health services research, the opportunities made available through the impressive advances of recent decades in the biomedical as well as the physical, computational and behavioral and social sciences have brought us to a frontier of unprecedented opportunity."*
- There is a dearth of reliable, integrated data on which to base priority setting decisions, including insufficient information on the human and financial costs of disease.

- Numerous areas of science continue to rapidly converge in conducting research, erasing the disease boundaries that had characterized such research in the past.

After consulting with scientific leaders within and outside NIH, and in order to meet these challenges while enhancing the priority setting process at NIH, I have decided that the Agency needs a new organization that will complement the existing process for determining strategic research initiatives. I have requested $2 million in the FY 2006 budget to establish this new entity, the Office of Portfolio Analysis and Strategic Initiatives, within the Office of the Director. This office will be charged with evaluating the entire Agency research portfolio to ensure that urgent public health needs are addressed in a timely way and that a sound decision support system is established that is based on rigorous and uniform sources of evidence.

Individual research grants remain the mainstay of NIH, and research in priority areas will always be awarded competitively. However, NIH also needs a global view of the totality of what we fund in our overall research portfolio. This new office will provide – with input from the Institutes and Centers and from the public, health care providers, policymakers, and scientists – tools that facilitate trans-NIH planning. It will drive data collection and sharing of information about research fields, diseases, and conditions, and collect and analyze data on the burden of disease. More effective analysis and management of our portfolio will lead to even better progress against disease.

An expanded approach to portfolio analysis will enable NIH to enhance the priority setting process while increasing coordination, identify appropriate cycles of change, maintain proper

turnover rates for grants and provide much more accountability to Congress and the public. Under such processes, in concert with the Institutes and Centers, we would identify crosscutting research that requires common investments from the various NIH Institutes and Centers. This approach must include a regular overview of all research so that we can have sufficient information to improve management of the entire NIH research portfolio.

My intent in creating the office is to have a transparent process and better decision-support tools characterized by a defined scope of review with broad input from the scientific community and the public; a solid, uniform database of information; an institutionalized process of regular trans-NIH evaluations; better tools for weighing scientific opportunity against public health urgency; and a process that enhances accountability to Congress, scientists, patients and the public at large.

The creation of the Office of Portfolio Analysis and Strategic Initiatives is an important step in the process I began when I became the NIH Director to increase collaboration among our 27 Institutes and Centers and to pool resources, where necessary, to expedite research and adapt to changes in scientific methods and new discoveries. Soon after becoming the NIH Director, in May 2002, I convened a series of scientific meetings to chart a "Roadmap for Medical Research" in the 21st century. Our purpose was to identify gaps and obstacles in biomedical research that no single institute at NIH could fill or overcome alone, but requires efforts by the entire Agency.

Three themes for the Roadmap were identified: Finding New Pathways to Discovery; Creating Research Teams of the Future; and Re-engineering the Clinical Research Enterprise. The

Roadmap is currently funding $235 million in this trans-NIH initiative and we have requested an additional $98 million for FY 2006.

The focus of the initiatives under New Pathways to Discovery is to build a better "toolbox" for medical researchers in the 21st century. By FY 2006, a network of Molecular Libraries Screening Centers will identify novel small molecules with potential as biochemical probes for investigating cellular pathways, and an Imaging Probe Development Center will be fully operational and servicing the extramural community.

Scientists need to move beyond the confines of their own discipline and explore new organizational models for team science. The initiatives within the Research Teams of the Future theme provide support to academic and research institutions that focus on creating interdisciplinary research training programs, workshops and courses for development of new scientists, new science teams, and new scientific inter-disciplines. In addition, specific support for high risk and innovative research will continue to be supported by the NIH Director's Pioneer Awards in FY2006.

The Re-engineering the Clinical Research Enterprise theme initiatives aim to integrate and strengthen clinical research networks and train multidisciplinary clinical researchers in order to accelerate clinical studies and trials. Efforts to inventory existing networks and test approaches to enhance informatics infrastructure will culminate in the launch of the National Electronic Clinical Trials and Research (NECTAR) network.

Implementation groups have been established to support each of the three themes. For example, under the initiative to find New Pathways to Discovery, there are separate groups for Building Blocks, Pathways and Networks; Molecular Libraries and Imaging; Structural Biology, Bioinformatics and Computational Biology; and Nanomedicine. These groups are funding such initiatives as National Technology Centers for Networks and Pathways; Molecular Libraries; a database of chemical structures; a core synthesis facility to produce imaging probes; and planning for nanomedicine centers.

Under the Research Teams of the Future theme, NIH is funding planning grants to establish Interdisciplinary Research Centers; an initiative to remove barriers to interdisciplinary research; and an initiative to facilitate public-private partnerships in science.

Projects are also underway in support of the third theme, Re-engineering the Clinical Research Enterprise. Initiatives include Harmonizing Regulatory requirements; integrating clinical research networks; and establishing core services for the translation of research findings.

The Roadmap has been a significant step in shifting the culture of NIH from single-purpose research funded by individual Institutes and Centers to research that will benefit all endeavors and is funded by multiple Institutes and Centers for the benefit of the entire Agency. NIH has been gradually moving in this direction for the last decade, but now we are advancing by leaps and bounds.

As an illustration of our responsiveness to emerging public health threats, NIH launched the

Strategic Plan for Obesity, a multi-disciplinary approach to addressing a burgeoning health crisis. There are 130 million obese American adults who are at risk of premature death, chronic illness, and reduction in quality of life. In addition, the obesity epidemic could cost the Nation $117 billion in medical costs and lost wages. Obesity is an example of a public health emergency that cannot be addressed by a single Institute, but must be a trans-NIH research initiative. We have 18 Institutes and Centers conducting research on such factors in the epidemic as behavioral, sociocultural, economic, environmental, genetic and biological causes.

NIH researchers have identified an elaborate network of hormones and other molecules that connect the brain, gastrointestinal tract, fat cells, and other parts of the body to achieve energy balance. An increased level of one of the appetite-induced hormones was found in obese people following diet-induced weight loss. It may explain why people have difficulty in maintaining weight loss. These hormones are now targets for the development of drug therapeutics.

This year, another important example of greater trans-NIH collaborations and coordination is the Neuroscience Blueprint. NIH has 15 Institutes conducting research on the brain, ranging from the National Institute of Neurological Disorders and Stroke to the National Institute of Mental Health to the National Institute on Drug Abuse. This set of diseases exacts a burden estimated to reach $500 billion in future years. By pooling funds and expertise, our Institutes will collaborate on research addressing some of the most prevalent causes of death and disability, including Parkinson's disease, ALS, Alzheimer's disease, spinal cord injury, dementia, hearing loss, eye disease, and muscular dystrophy. The Blueprint will conduct research on economies of scale and train the next generation of neuroscientists.

These are prominent examples of how NIH is adapting to the need for new approaches to medical research. Another example includes collaboration on modeling simple organisms used in pre-clinical research, such as the mouse, the rat, budding yeast, the fruit fly, and the zebrafish. Also, NIH supports trans-NIH initiatives on health disparities research, liver disease, autism, pain research, biodefense, and imaging.

We will continue to facilitate trans-NIH research and assess priorities in response to public health urgencies and scientific requirements. However, the mainstays of NIH – peer review and investigator-initiated research – are the cornerstones of our success. This should be enhanced and not weakened. But with this in mind, NIH will continue to seek the best ways of funding the whole continuum of medical research with the ultimate goal of diagnosing, preventing, treating, and curing disease.